Esomeprazole 40 mg Provides More Effective Intragastric Acid Suppression At Steady State Than Standard Doses of Other Proton Pump Inhibitors

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CONCLUSIONS

- **Esomeprazole 40 mg once daily provided significantly more hours in a 24-hour period of intragastric acid suppression at steady state compared with standard doses of lansoprazole, omeprazole, pantoprazole or rabeprazole in patients with GERD.**
- **Intragastric pH was maintained at >4.0 for 12 or more hours in a significantly larger percentage of patients treated with standard dose esomeprazole relative to all other proton pump inhibitors.**

1. BACKGROUND

- Proton pump inhibitors owe their clinical efficacy to their ability to suppress gastric acid secretion via the inhibition of H^+/K^+-adenosine triphosphatase in gastric parietal cells.[1]
- Esomeprazole, the first proton pump inhibitor developed as a single optical isomer, has an enhanced pharmacodynamic and pharmacokinetic profile. This results in a more effective and longer lasting inhibition of gastric acid secretion over the 24-hour dosing period.
- Intragastric acid suppression is the most direct measure of the pharmacodynamics of proton pump inhibitors. The number of hours in a 24-hour period that intragastric pH is >4.0 is one of the key parameters used to assess the effects of proton pump inhibitors,[1-4] and has clinical relevance for the treatment of GERD.
- Mucosal healing rates in erosive esophagitis can be correlated with the duration that intragastric pH is maintained above 4.0.[5]
- To date, no single study has compared the pharmacodynamics of the standard doses of all available proton pump inhibitors.

2. OBJECTIVE

- To compare the effect of standard doses of esomeprazole versus standard doses of omeprazole, lansoprazole, pantoprazole and rabeprazole on 24-hour intragastric pH at steady state.

3. METHODS

- A randomized, single-center, open-label, 5-way crossover study was conducted to determine the 24-hour intragastric pH profile following 5 days of once-daily oral PPI administration.
- Patients between 18 to 60 years of age who experienced heartburn for an average of at least 2 days per month during the 2 months prior to screening were eligible for enrollment.
- Patients received esomeprazole 40 mg, lansoprazole 30 mg, omeprazole 20 mg, pantoprazole 40 mg or rabeprazole 20 mg orally, once daily on 5 consecutive mornings, 30 minutes prior to a standardized breakfast. Each treatment period was separated by a washout period of 10–17 days during which no PPI was taken.
- Patients were randomly assigned to receive the comparators in one of five sequences. Patients must have completed all five treatment periods to have been considered evaluable.
- A calibrated electrode attached to a Medtronic Digitrapper™ pH data logger (Medtronic; Shoreview, MN) was positioned 10 cm distal to the manometrically located lower esophageal sphincter and used to evaluate intragastric pH every 4 seconds for 24 hours beginning immediately before the dose on day 5.
- The primary pharmacodynamic end point of this study was the number of hours in a 24-hour period that intragastric pH of each study drug was >4.0 on day 5 of treatment. The least squares mean and standard error of the mean were calculated for each treatment group using a mixed model analysis of variance with effects for subject, period and treatment, in which subject is random effect.
- Secondary end points included between-treatment differences in the 24-hour mean pH on day 5 and the percentage of patients with pH >4.0 for 12 or more hours.
- *P* values for the percentage of patients with pH >4.0 for 12 or more hours were analyzed using a repeated measurement logistic model with effects for subject, period, and treatment.
- It was calculated that 30 evaluable patients would be required to provide 95% overall power to detect a difference of 12.4% (3 hours) between esomeprazole 40 mg once daily and any of the other four comparators.

4. RESULTS

- Baseline demographic and clinical characteristics of the 34 evaluable patients are summarized in Table 1.

Table 1. Baseline Demographics and Clinical Characteristics (Evaluable Cohort; N = 34)

Female gender, n (%)	26.0	(76.5)
Age, y, Mean (SD)	44.1	(11.0)
Caucasian race, n (%)	31.0	(91.2)
Height, cm, Mean (SD)	167.6	(8.5)
Weight, kg, Mean (SD)	83.2	(18.1)
Body mass index, kg/m², Mean (SD)	29.4	(5.1)
Heartburn ≥3 times/wk, n (%)	23.0	(67.6)

SD = standard deviation

- All five treatment groups had a mean of greater than 23.75 hours of evaluable data.
- The mean number of hours on day 5 that intragastric pH was >4.0 is shown in Figure 1. Treatment with esomeprazole provided significantly more hours with intragastric pH >4.0 compared with all other proton pump inhibitors.
- A statistically significant increase in mean pH was demonstrated for esomeprazole 40 mg once daily compared with all of the other proton pump inhibitors (Table 2).
- A significantly higher percentage of patients had an intragastric pH >4.0 for ≥12 hours during treatment with esomeprazole than

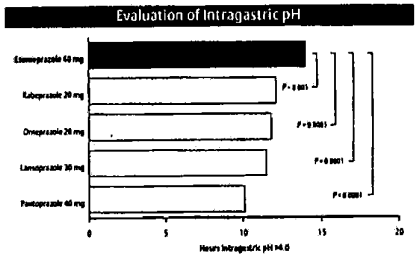

Figure 1. Mean number of hours on day 5 that intragastric pH was >4.0 by treatment group (N = 34).

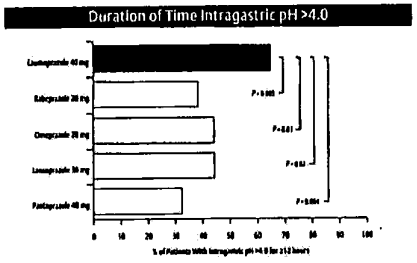

Figure 2. Percent of patients with intragastric pH >4.0 for ≥12 hours (N = 34).

Table 2. Mean 24-hour Intragastric pH on Day 5 by Treatment Group (N = 34)

Treatment	Mean pH (SEM)
Esomeprazole 40 mg	4.04 (0.16)*
Rabeprazole 20 mg	3.70 (0.17)
Omeprazole 20 mg	3.54 (0.17)
Lansoprazole 30 mg	3.56 (0.15)
Pantoprazole 40 mg	3.33 (0.17)

SEM = standard error of the mean.

* $P < 0.0001$ for comparison between esomeprazole versus lansoprazole, omeprazole and pantoprazole; $P = 0.003$ for comparison between esomeprazole and rabeprazole.

5. REFERENCES

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Supported by a grant from AstraZeneca LP, Wilmington, DE, USA